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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,580	11/14/2003	Paul Wentworth	TSRI 784 5	1792

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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06/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/714,580	WENTWORTH ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2007 and 16 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-42,44,45 and 48-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-42,44,45 and 48-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed April 9, 2007 has been entered. The examiner acknowledges the amendments to the specification. Claim 40 has been amended. Claims 1-39, 43 and 46-47 are cancelled. Claims 48-58 have been newly added. Claims 40-42, 44-45 and 48-58 are under consideration in this office action.

Priority

2. Applicant's claim for domestic priority to provisional application US 60/426,242 under 35 U.S.C. 119(e) is acknowledged.

Withdrawal of Rejections

3. The following rejections have been in view of applicants' amendments and arguments:

a) The rejection of claims 40-43 and 45 under 35 U.S.C. 102(b) as being anticipated by Berthiaume et al.

b) The rejection of claims 46-47 under 35 U.S.C. 102(b) as being anticipated by Wentworth et al., in light of the Scripps Press Release of November 14, 2002.

Response to Arguments

4. Applicant's arguments filed July 16, 2007 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The rejection of claims 40-42, 48-51 and 54-56 under 35 U.S.C. 102(b) as being anticipated by Devanathan et al., is maintained for reasons already of record. The rejection Devanathan et al., teach a method of generating a reactive oxygen species to inhibit the growth of a bacterium comprising contacting the microbe with (i) an antibody that can bind to the bacterium and (ii) a source of singlet oxygen is a sensitizer molecule wherein the source of the singlet oxygen is not covalently attached to the antibody and the source of the singlet oxygen would not on it own, inhibit the growth of the bacteria when exposed to light.

Applicant considers that the rejection has been overcome, because of the negative limitation that "the source of singlet oxygen is not covalently attached to the antibody." However the claim can be read as encompassing precisely what Devanathan et al., teach. The rabbit IgG antibodies against *E. coli* are clearly not covalently attached to the diiodofluorescein sensitizer; rather, the sensitizer is indirectly bound to the rabbit IgG antibodies in the double antibody targeting method of Devanathan et al., (page 2981, last full para.). According, the antibody corresponds to the rabbit IgG antibodies against *E. coli*. The fact that the sensitizer of Devanathan et al., is conjugated to a third element, namely a goat anti-rabbit IgG antibody, does not detract

from the basis of rejection because the claim scope is open to the inclusion of any additional element, due to the recitation of "comprising." Thus the claims are anticipated by Devanathan et al.

Applicants' urge that Devanathan et al., is limited, since the claims recite that the source of singlet oxygen would not on its own inhibit the growth of the bacteria. However it is the examiner's position that Devanathan is not limited by its teaching of photodynamic sensitizers. Devanathan et al., teach that for photodynamic killing of microorganism, the combination of light, oxygen and absorbing dyes called photodynamic sensitizers are essential. Thus the source of singlet oxygen, being the photodynamic sensitizer would not, on its own, inhibit the growth of bacteria contrary to applicants' statement.

Furthermore, it is noted that the interpretive "wherein" clause as recited in the claims does not recite any additional active method steps, but simply states a characterization. Therefore the "wherein" clause is not considered to further limit the method defined by the claims and has not been given patentable weight in construing the claims. See *Texas Instruments, Inc. v. Int'l Trade Comm'n*, 988 F.2d 1165, 26 USPQ2d 1018 (Fed. Cir. 1993). Applicants' arguments are not persuasive , therefore the rejection is maintained.

8. The rejection of claims 40-42, 44-45 and 48-58 under 35 U.S.C. 102(b) as being anticipated by Wentworth et al., in light of the Scripps Press Release of November 14, 2002 is maintained.

At the outset, the examiner sets forth that M.P.E.P. section 2131.01 entitled Multiple Reference 35 U.S.C. 102 Rejections states that a 35 U.S.C. 102 rejection over multiple references has been held to be proper when the extra reference is cited to show that a characteristic not disclosed in the reference is inherent.

The claims are drawn to a method of generating a reactive oxygen species to inhibit the growth of a bacterium comprising contacting the microbe with (i) an antibody that can bind to the bacterium and (ii) a source of singlet oxygen is a sensitizer molecule wherein the source of the singlet oxygen is not covalently attached to the antibody and the source of the singlet oxygen would not on it own, inhibit the growth of the bacteria when exposed to light. The dependant claims are drawn to specific sources for the singlet oxygen, the types of antibodies and the reactive species generated.

Wentworth et al., (PNAS, 2000) teach antibodies have the intrinsic capacity to destroy antigens. Antibodies have the capacity to convert molecular oxygen into hydrogen peroxide, thereby effectively linking recognition and killing events (page 10,930). Wentworth et al., disclosed this capability with whole antibodies and $F(ab')_2$ fragments (see the materials and methods section). The sensitization and quenching assays teach a solution of horse IgG antibody and sensitizer molecule, hematopophyrin were placed in proximity to a strip of light and the concentration of hydrogen peroxide produced was determined (page 10,930). Wentworth et al., teach that superoxide anion radicals are the direct precursor of hydrogen peroxide and the toxic derivatives it spawns, such as hydroxyl radials (HO*). Thus Wentworth et al., teach that the reactive oxygen species generated is a superoxide radical, hydroxyl radical or hydrogen

peroxide. It is noted that the art is silent with respect to the generation of an ozone as a reactive oxygen species.

However, the Scripps Press Release inherently teaches the production of ozone by antibodies during bacterial killing has played an hitherto unknown role in immune protection (Scripps Press Release). The ozone is part of a previously unrecognized killing mechanism that enhances the defensive role of antibodies by allowing them to subject pathogens to hydrogen peroxide and participate directly in their killing. Antibodies produce the chemical oxidant hydrogen peroxide which is lethal to bacterial cells because it pokes holes in their cell walls, bursting the cells and killing them. The antibodies reduce singlet oxygen and produce ozone as a side product. The authors state that all antibodies have the ability to do this. Therefore the generation of hydrogen peroxide and ozone as a side product, are inherent abilities that antibodies have. Thus, the Scripps Press Release teach that inherently, antibodies will generate ozone as a reactive species which will inhibit the growth of a bacterial microbe.

Applicants assert that the Scripps Press Release is not prior art in light of the November 14, 2002 date. However, a reference, such as the Scripps Press Release, may be used for its teachings of the inherent mechanisms/features irrespective of whether or not it can be cited as prior art. See MPEP 2112, Sect. II. Therefore applicants' assertion is not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. The new matter rejection of claims 40-42, 44, 45 and 54-58 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

The rejection was on the grounds that neither the specification nor originally presented claims provides support for a method of generating a reactive oxygen species to inhibit the growth of a bacterium comprising contacting the bacterium with (i) an antibody or antibody fragment that can bind to the bacterium and (ii) a source of singlet oxygen wherein the source of singlet oxygen is not covalently attached to the antibody.

Applicant did not point to support in the specification for the instantly claimed method. Applicants point to Example III, The Bactericidal Assays beginning at pages 77 for support. Applicants' alleged that because hematoporphyin IX and antibody were added at different concentration and Figures 14A-D illustrate killing of bacteria by antibodies; the specification provides support for the source of singlet oxygen not being covalently attached to the antibody. However neither Example III nor Figures 14A-D make any reference to the antibody not being covalently bound to the singlet oxygen. Applicants points to page 25,line 4 which states that in some embodiments the sensitizer is not conjugated to the antibody. However, conjugation is not equivalent to

covalent bonding. A covalent bond is a form of chemical bonding that is characterized by the *sharing* of pairs of electrons between atoms, or between atoms and other covalent bonds. Antibody conjugation utilizes chemical linkages to associate the antibody with another moiety. Thus, the teaching of antibody conjugation does not disclose the source of singlet oxygen is not covalently attached to the antibody.

There is no discussion of covalent bonds. Therefore, applicant failed to specifically point to support for a source of singlet oxygen is not covalently attached to the antibody. Accordingly, it appears that there is no support in the specification. Therefore, applicants must specifically point to page and line number support for a method of generating a reactive oxygen species to inhibit the growth of a bacterium comprising contacting the bacterium with (i) an antibody or antibody fragment that can bind to the bacterium and (ii) a source of singlet oxygen, wherein the source of singlet oxygen is not covalently attached to the antibody as recited by the claims. Therefore, applicants' argument is not persuasive and the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 40-42, 44, 45 and 48-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claims 40, 48 and 54 recites the limitation "the microbe" in the claims. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 48-51 and 53 are rejected under 35 U.S.C. 102 (b) as being anticipated by Berthiaume et al (Biotechnology. 1994. Vol. 12:703-706).

The claims are drawn to a method of generating a reactive oxygen species to inhibit the growth of a bacterium comprising contacting the bacterium with (i) an antibody that can bind to the microbe and (ii) a source of singlet oxygen to thereby generate ozone to inhibit the growth of the bacterium, wherein the source of singlet oxygen would not , on its own, inhibit the growth of the bacteria when exposed to light. The dependant claims are drawn to specific sources for the singlet oxygen, the sensitizer molecule, the attachment of the molecule and antibody, and the type of fragmented antibodies.

Berthiaume et al., teach antibody-targeted photolysis of bacteria *in vivo*. Berthiaume et al., teach the development an antibody-targeted photolysis method which uses antibody bound photosensitizers which are toxic only upon activation of light (page 703). Berthiaume et al., teach bacterial killing *in vitro* using tin (IV) chlorine e_6 as the

photosensitizer was shown to be highly efficient in the production of singlet oxygen and other short-lived species (page 703). Thus Berthiaume et al., teach sensitizer molecules as the source of the singlet oxygen. The results of this study show that specific tin (IV) chlorine e_6-monoclonal antibody conjugates directed against *P. aeruginosa* can specifically kill more than 75% of the bacteria (page 703). Berthiaume et al., teach transport studies of antibody fragments have shown improved and rapid infiltration of the selected target sites (page 705).

Therefore, Berthiaume et al., teach a method of generating a reactive oxygen species to inhibit the growth of a bacterium.

Conclusion

12. No claims allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Shanon Foley, can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/

Primary Examiner, Art Unit 1645